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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,822	03/19/2004	Lawrence W. Stanton	135/003P	7106

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GERON CORPORATION
230 CONSTITUTION DRIVE
MENLO PARK, CA 94025

EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 11/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/804,822	STANTON ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *8,9,13,15 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,10-12,14 and 17-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of group I, claims 1-7, 10-12, 14 and 17-20, in the reply filed on 10-13-06 is acknowledged.

2. Claims 8, 9, 13, 15 and 16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10-13-06.

Claims 1-20 are pending. Claims 1-7, 10-12, 14 and 17-20 are under consideration.

Priority

3. If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 120, a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

If the instant application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months

from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

On page 1 of the specification under "Reference to Related Applications", application numbers for the two PCT applications have not been disclosed. It appears that the filing date for one of PCT applications is 3-13-04 rather than 3-15-04. Further,), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. Appropriate correction is required.

Claim Objections

4. Claim 18 is objected to because of the following informalities: The phrase (hTERT) Oct3/4" in line 3 of claim 18 appears to be a typographical error. A comma "," is needed in between "(hTERT)" and "Oct ¾". Appropriate correction is required.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7, 10-12 and 14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5, 6, 11, 12, 47 and 48 of copending Application No. 10/388,578. Although the conflicting claims are not identical, they are not patentably distinct from each other because although drawn to different scope, they encompass the same invention and obvious variants thereof.

Claims 1-7, 10-12 and 14 of instant invention are directed to a method for determining the extent of differentiation in a population of isolated human embryonic stem (hES) cells comprising detecting or measuring two or more markers preferentially expressed in undifferentiated hES cells and one or more markers preferentially expressed after differentiation of hES cells.

Claims 1, 5, 6, 11, 12, 47 and 48 of Application No. 10/388,578 are directed to a method comprising detecting or measuring expression of two or more, or three or more, of the markers in any of Tables 5-9 in a population of primate pluripotent stem cells, such as human embryonic stem cells, in vitro via PCR amplification or antibody assay.

The primate pluripotent stem cells encompass human embryonic stem cells and the markers in Tables 5-9 contain genes that are down-regulated or up-regulated after differentiation. Thus, it would have been obvious for one of ordinary skill in the art at the time of the invention to practice the claimed invention of the instant application according to the teachings of Application No. 10/388,578.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 3, 4 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "at least one of the markers ... selected from ... and the markers detected by antibodies Tra-1-60 and Tra-1-81" in claim 3 is vague and renders the claim indefinite. The markers detected by antibodies Tra-1-60 and Tra-1-81 are more than one marker. It is unclear how "at least **one** of the markers" could be "the **markers** detected by antibodies Tra-1-60 and Tra-1-81".

The term "SSEA-4" in claim 3 is vague and renders the claim indefinite. The term "SSEA-4" is an abbreviation and can stand for various meanings. It is unclear what meaning is intended. Spelling out the term "SSEA-4" would be remedial.

The term "SSEA-3" in claim 4 is vague and renders the claim indefinite. The term "SSEA-3" is an abbreviation and can stand for various meanings. It is unclear what meaning is intended. Spelling out the term "SSEA-3" would be remedial.

The term "STRO-1" in claim 7 is vague and renders the claim indefinite. The term "STRO-1" is an abbreviation and can stand for various meanings. It is unclear what meaning is intended. Spelling out the term "STRO-1" would be remedial.

8. Claims 1-7, 10-12, 14 and 17-20 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: whether the extent of differentiation is determined or not after the markers are detected or measured. The method step fails to refer back to the preamble of the claimed method, i.e. determining the extent of differentiation.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-7, 10-12, 14 and 17-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-7, 10-12, 14 and 17-20 are directed to a method for determining the extent of differentiation in a population of isolated human embryonic stem (hES) cells comprising detecting or measuring two or more markers preferentially expressed in undifferentiated hES cells and one or more markers preferentially expressed after differentiation of hES cells, and a system for assessing a culture of undifferentiated hES cells or their progeny comprising antibody specific for three or more markers, of which at least two are preferentially expressed in undifferentiated hES cells, and at least one is preferentially expressed in stromal cells. Claim 2 specifies the markers preferentially expressed in undifferentiated hES cells is selected from

Cripto, GRP receptor, PODXL and hTERT. Claim 3 specifies at least one of the markers preferentially expressed in undifferentiated hES cells is selected from Oct ¾, SSEA-4, and the markers detected by antibodies Tra-1-60 and Tra-1-81. Claim 4 specifies measuring three or more markers preferentially expressed in undifferentiated hES cells selected from hTERT, Oct ¾, Cripto, GRP, PODXL, SSEA-3, SSEA-4, Tra-1-60 and TRa-1-81. Claim 5 specifies detecting or measuring hTERT, Oct ¾, and a marker selected from Cripto, SSEA-4, Tra-1-60 and Tra-1-81. Claims 6 and 7 specify at least one of the markers preferentially expressed after differentiation of the hES cells is a stromal cell markers as recited in the claim. Claims 10-12 specify expression of the marker is detected by antibody assay including flow cytometry using flrorescence-labeled antibody and immunocytochemistry. Claim 14 specifies further quantifying the proportion of undifferentiated hES cells or differentiated cells in the culture from positive expression of the undifferentiated cell markers and lack of expression of the stromal cell markers.

The specification discloses a plurality of marker genes that appear to be more abundantly expressed in undifferentiated hES cell lines when compared to that in differentiated hES cell lines (i.e. differentiated hES cell lines that have been induced to differentiate to embryoid body (EB) formation, exposure to retinoid acid to differentiate to neuronal precursor cells, and exposure to DMSO to differentiate to hepatocyte precursor cells). The specification discloses a plurality of marker genes that appear to be less abundantly expressed in undifferentiated hES cell lines as compared to that in differentiated hES cell lines (Examples 1-3, Table 2 and 3).

The claims encompass determining the extent of differentiation in a population of hES cells by detecting or measuring two or more markers of any type or recited in the claims

preferentially expressed in undifferentiated hES cells and/or one or more markers of any type or recited in the claims preferentially expressed in differentiated hES cells. The claims also encompass a system for assessing a culture of undifferentiated hES cells or their progeny comprising antibody specific for three or more markers of any type or recited in the claims, of which at least two are preferentially expressed in undifferentiated hES cells, and at least one is preferentially expressed in stromal cells. The specification fails to provide adequate guidance and evidence for how to determine the extent of differentiation in a population of isolated hES cells by detecting two or more markers of undifferentiated hES cells and only one or more than one marker for differentiated hES cells. The specification also fails to provide adequate guidance and evidence for how to assess a culture of undifferentiated hES cells or their progeny by using antibodies specific for at least two markers of undifferentiated hES cells and at least one marker for stromal cells.

Pera et al., 2001 (WO 01/68815 A1) points out that human pluripotential stem cells express SSEA-3, SSEA-4, Tra 1-60, GCTM-2, alkaline phosphatase and Oct-4 (e.g. p.3). However, there is no evidence of record that shows any two or more of those markers or any marker would be able to define the undifferentiated state of the hES cells. Mayer-Proschel et al., 2002 (Clinical Neuroscience Research, Vol. 2, p. 58-69) identified multipotent human neuroepithelial precursor cells (hNEPs) and demonstrates that "hNEPs constitute a small fraction of the cells present at any stage examined and three additional dividing populations can be identified based on expression of epitopes recognized by E-NCAM, A2B5 and CD44. E-NCAM+ cells co-express neuronal markers and can differentiate into multiple classes of neurons. Two types of A2B5+ cells can be distinguished: a small neuronal population that co-

express E-NCAM immunoreactivity and a larger glial population that is E-NCAM negative. CD44+ cells do not express neuronal markers or oligodendrocyte markers but co-express astrocytic markers and likely represent an astrocyte precursor cell" (e.g. abstract). It appears that there are several different types of neural precursor cells expressing different markers. Differentiated hES cells encompass not only neuronal precursor cells but also numerous different precursor cells or multipotent stem cells including hematopoietic stem cells, follicular precursor cells, and pancreatic stem cells etc. Each precursor cells or multipotent stem cells would also encompass different differentiated stages expressing different markers. The ES, EB, preHEP and preNEU in Tables 2 and 3 of the specification only represent particular undifferentiated and differentiated stages of hES cells. The specification fails to provide specific guidance for how to use the data provided in Tables 2 and 3 to determine or define numerous different undifferentiated stages, i.e. extent of differentiation, of hES cells and numerous different differentiated stages of various precursor cells or multipotent stem cells. One skilled in the art at the time of the invention would not know how to define or determine the extent of differentiation of the hES cells or assessing a culture of undifferentiated hES cells by merely detecting or measuring at least two markers preferentially expressed in undifferentiated hES cells, and at least one marker preferentially expressed in stromal or differentiated cells.

Further, the data shown in Tables 2 and 3 of the specification are expression levels of cDNA rather than protein expression levels. Expression levels of cDNA or mRNA do not necessarily correspond to the expression level of protein since there are post-transcription regulation of mRNA and post-translational regulation of protein. The specification fails to provide adequate guidance and evidence for whether the expression levels of cDNA of different

genes at different differentiated stage of the hES cells could be translated into expression levels of proteins encoded by those different genes. Thus, one skilled in the art at the time of the invention would not know how to use antibody assay to define or determine the extent of differentiation of hES cells as claimed.

None of the claims contain any recitation about whether the plurality of marker genes is to be highly expressed, moderately expressed or not expressed at all and there is no correlation between the expression pattern of protein via antibody assay and the extent of differentiation or assessing any cell culture. The specification fails to provide specific guidance for what level of expression pattern would be sufficient to define or determine the extent of differentiation of hES cells or to assess any cell culture. Therefore, one skilled in the art at the time of the invention would not know how to practice the claimed invention.

In addition, the specification discloses a plurality of marker genes that appear to be differentially expressed in three different undifferentiated hES cell lines when compared to that in particular differentiated hES cell lines. The claims read on determining the extent of differentiation of any isolated hES cell or assessing any culture of undifferentiated hES cells or their progeny. Each hES cell line is derived from individual organisms with distinct genetic backgrounds. The art of record at the time of the invention teaches that variation in DNA sequence are common in human genome. Kruglyak et al., 2001 (Nature Genetics, Vol. 27, p. 234-236) teaches that every person on the planet, with the exception of identical twins, has a unigue genome and two human genome differ at 1 nucleotide per 1,331 bp (e.g. p. 234, left column and right column). Therefore, the hES cell lines derived from different human embryos would carry thousands of genetic variations. As such, it was unpredictable at the time of the

invention whether the gene expression profiles or protein expression profiles of the undifferentiated or differentiated hES cell lines (or their progeny) would be identical.

For the reasons set forth above, one skilled in the art at the time of the invention would have to engage in undue experimentation to practice over the full scope of the invention claimed. This is particularly true based upon the nature of the claimed invention, the state of the art, the unpredictability found in the art, the teaching and working examples provided, the level of one of ordinary skill which is high, the amount of experimentation required, and the breadth of the claims.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1, 3, 4, 6, 7, 10 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Pera et al., 2001 (WO 01/68815 A1).

Claims 1, 3, 4, 6, 7, 10 and 12 are directed to a method for determining the extent of differentiation in a population of isolated human embryonic stem (hES) cells comprising detecting or measuring two or more markers preferentially expressed in undifferentiated hES cells and one or more markers preferentially expressed after differentiation of hES cells. Claim 3 specifies at least one of the markers preferentially expressed in undifferentiated hES cells is selected from Oct ¾, SSEA-4, and the markers detected by antibodies Tra-1-60 and Tra-1-81.

Claim 4 specifies measuring three or more markers preferentially expressed in undifferentiated hES cells selected from hTERT, Oct ¾, Cripto, GRP, PODXL, SSEA-3, SSEA-4, Tra-1-60 and TRa-1-81. Claims 6 and 7 specify at least one of the markers preferentially expressed after differentiation of the hES cells is a stromal cell markers as recited in the claim. Claims 10 and 12 specify expression of the marker is detected by antibody assay, for example, immuno-cytochemistry.

Pera et al., 2001 (WO 01/68815 A1) points out that human pluripotential stem cells express SSEA-3, SSEA-4, Tra 1-60, GCTM-2, alkaline phosphatase and Oct-4 (e.g. p.3). Pera teaches a method of producing an enriched preparation of human ES derived neural progenitor cells comprising obtaining an undifferentiated hES cells, inducing somatic differentiation of the ES cells to a neural progenitor cell and identifying a neural progenitor cell by expressed markers of primitive neuroectoderm and meural stem cells such as polysialyated N-CAM, nestin and vimentin. Pera teaches an undifferentiated human ES cell is immunoreactive with markers for human pluripotent stem cells including SSEA-4, GCTM-2 antigen, and TRA 1-60 (e.g. Example 2, p. 80, claim 4). Pera further teaches evaluation of the proportion of cells in the spheres, which are generated from differentiating ES cells, that expressed polysialyated NCAM, nestin and vimentin by using antibody against polysialyated NCAM (e.g. bridging p. 73-74). Thus, claims 1, 3, 4, 6, 7, 10 and 12 are anticipated by Pera.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 1, 14 and 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pera et al., 2001 (WO 01/68815 A1).

Claims 1, 14 and 17-20 are directed to a method for determining the extent of differentiation in a population of isolated human embryonic stem (hES) cells comprising detecting or measuring two or more markers preferentially expressed in undifferentiated hES cells and one or more markers preferentially expressed after differentiation of hES cells, and a system for assessing a culture of undifferentiated hES cells or their progeny comprising antibody specific for three or more markers, of which at least two are preferentially expressed in undifferentiated hES cells, and at least one is preferentially expressed in stromal cells. Claim 14 specifies further quantifying the proportion of undifferentiated hES cells or differentiated cells in the culture from positive expression of the undifferentiated cell markers and lack of expression of the stromal cell markers.

Pera et al., 2001 (WO 01/68815 A1) points out that human pluripotential stem cells express SSEA-3, SSEA-4, Tra 1-60, GCTM-2, alkaline phosphatase and Oct-4 (e.g. p.3). Pera teaches a method of producing an enriched preparation of human ES derived neural progenitor cells comprising obtaining an undifferentiated hES cells, inducing somatic differentiation of the ES cells to a neural progenitor cell and identifying a neural progenitor cell by expressed markers of primitive neuroectoderm and meural stem cells such as polysialyated N-CAM, nestin and vimentin. Pera teaches an undifferentiated human ES cell is immunoreactive with markers for human pluripotent stem cells including SSEA-4, GCTM-2 antigen, and TRA 1-60 (e.g. Example 2, p. 80, claim 4). Pera further teaches evaluation of the proportion of cells in the spheres, which are generated from differentiating ES cells, that expressed polysialyated NCAM, nestin and vimentin by using antibody against polysialyated NCAM (e.g. bridging p. 73-74), and a neural progenitor cell does not express Oct-4 (e.g. p. 82).

Pera does not specifically teach quantifying the proportion of undifferentiated hES cells or differentiated cells in the culture from positive expression of the undifferentiated cell markers and lack of expression of the stromal cell markers, and a system or kit comprising antibodies specific to the undifferentiated and differentiated hES cell markers.

Since Pera teaches detection of undifferentiated or differentiated hES cell markers via antibody assay and evaluation of the proportion of cells in the spheres, which are generated from differentiating ES cells, that expressed polysialyated NCAM, nestin and vimentin by using antibody against polysialyated NCAM, and a neural progenitor cell does not express Oct-4, therefore, it would have been obvious for one of ordinary skill in the art at the time of the invention to quantify the proportion of undifferentiated hES cells or differentiated cells in the

culture from positive expression of the undifferentiated cell markers and lack of expression of the stromal cell markers. It also would have been obvious for one of ordinary skill in the art to prepare a system or kit comprising the antibodies specific to the undifferentiated and differentiated hES cell markers because Pera teaches detection of undifferentiated or differentiated hES cell markers via antibody assay and a method of producing an enriched preparation of human ES derived neural progenitor cells comprising identifying a neural progenitor cell by expressed markers.

One having ordinary skill at the time the invention was made would have been motivated to do so in order to produce an enriched preparation of human ES derived neural progenitor cells or to evaluate the proportion of cells in the spheres generated from differentiating ES cells that expressed polysialyated NCAM, nestin and vimentin with reasonable expectation of success.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shin-Lin Chen, Ph.D.

/schen/

SHIN-LIN CHEN
PRIMARY EXAMINER